

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

At page 1, line 3, between the title and the Background of the Invention section, please insert the following paragraph:

--This application is a continuation of pending U.S. Serial No. 09/347,114, filed on July 2, 1999.--

In the Claims:

Please cancel Claims 1-81, 87, 88, 90, and 94 without prejudice.

VERSION WITH MARKINGS TO SHOW CHANGES MADEIn the Specification:

At page 1, lines 1-2, please delete the title and insert therefor the following new title:

--[GENETIC TEST TO DETERMINE NON-RESPONSIVENESS TO STATIN DRUG
TREATMENT]OLIGONUCLEOTIDE PRIMER SEQUENCES, PRIMER SETS, AND
GENETIC TESTING KITS FOR LIPOPROTEIN LIPASE GENE ALLELES--.

At page 1, line 3, between the title and the Background of the Invention section, please delete the paragraph and insert therefor the following paragraph:

--This application is a continuation of U.S. Serial No. 09/347,114, filed on July 2, 1999, which issued as U.S. Patent No. 6,297,014, on October 2, 2001--.

In the Claims:

Please cancel Claims 82 and 83, without prejudice. Please amend Claims 84-86, 89, 91-93, and 95-102, and add new Claims 103-117, as follows.

84. (Amended) An oligonucleotide primer for detecting a genetic predisposition for non-responsiveness to statin drug treatment in a human, said primer having a nucleotide sequence consisting of [sequence] 5'-GCA TCT GCC TTC AGC TAG ACA TTG-3' (SEQ. ID. NO. 1).

85. (Amended) An oligonucleotide primer for detecting a genetic predisposition for non-responsiveness to statin drug treatment in a human, said primer having a nucleotide sequence consisting of [sequence] 5'-TCT TCC AGA AGG GTG AGA TTC CAA-3' (SEQ. ID. NO.:2).

86. (Twice Amended) An oligonucleotide primer for detecting a genetic predisposition for non-responsiveness to statin drug treatment in a human, said primer having a nucleotide sequence consisting [essentially of a nucleotide sequence] of (SEQ. ID. NO.:1), (SEQ. ID. NO.:2), (SEQ. ID. NO.:3), (SEQ. ID. NO.:4), (SEQ. ID. NO.:5), (SEQ. ID. NO.:6), (SEQ. ID. NO.:7), (SEQ. ID. NO.:8), (SEQ. ID. NO.:9), (SEQ. ID. NO.:10), (SEQ. ID. NO.:11), (SEQ. ID. NO.:12), (SEQ. ID. NO.:13), (SEQ. ID. NO.:14), (SEQ. ID. NO.:15), (SEQ. ID. NO.:16), (SEQ. ID. NO.:17), (SEQ. ID. NO.:18), (SEQ. ID. NO.:19), (SEQ. ID. NO.:20), (SEQ. ID. NO.:21), (SEQ. ID. NO.:22), (SEQ. ID. NO.:23), (SEQ. ID. NO.:24), (SEQ. ID. NO.:25), (SEQ. ID. NO.:26), (SEQ. ID. NO.:27), (SEQ. ID. NO.:28), (SEQ. ID. NO.:29), (SEQ. ID. NO.:30), (SEQ. ID. NO.:31), (SEQ. ID. NO.:32), (SEQ. ID. NO.:35), (SEQ. ID. NO.:36), (SEQ. ID. NO.:37), (SEQ. ID. NO.:38), (SEQ. ID. NO.:39), (SEQ. ID. NO.:40), (SEQ. ID. NO.:41), (SEQ. ID. NO.:42), (SEQ. ID. NO.:43), (SEQ. ID. NO.:44), (SEQ. ID. NO.:45), (SEQ. ID. NO.:46), (SEQ. ID. NO.:47), (SEQ. ID. NO.:48), (SEQ. ID. NO.:49), (SEQ. ID. NO.:50), (SEQ. ID. NO.:51), (SEQ. ID. NO.:52), (SEQ. ID. NO.:53), (SEQ. ID. NO.:54), (SEQ. ID. NO.:55), (SEQ. ID. NO.:56), (SEQ. ID. NO.:57), (SEQ. ID. NO.:58), (SEQ. ID. NO.:59), (SEQ. ID. NO.:60), (SEQ. ID. NO.:61), (SEQ. ID. NO.:62), (SEQ. ID. NO.:63), (SEQ. ID. NO.:64), (SEQ. ID. NO.:65), (SEQ. ID. NO.:66), (SEQ. ID. NO.:67), (SEQ. ID. NO.:68), (SEQ. ID. NO.:69), (SEQ. ID. NO.:70), (SEQ. ID. NO.:71), (SEQ. ID. NO.:72), (SEQ. ID. NO.:73), (SEQ. ID. NO.:74), (SEQ. ID. NO.:75), (SEQ. ID. NO.:76), (SEQ. ID. NO.:77), (SEQ. ID. NO.:78), or (SEQ. ID. NO.:79).

89. (Twice Amended) An oligonucleotide primer for detecting a genetic predisposition for non-responsiveness to statin drug treatment in a human, said primer having a nucleotide sequence consisting [essentially of a nucleotide sequence] of (SEQ. ID. NO.:82), (SEQ. ID. NO.:83), (SEQ. ID. NO.:84), (SEQ. ID. NO.:85), (SEQ. ID. NO.:86), [(SEQ. ID. NO.:87),] (SEQ. ID. NO.:88), (SEQ. ID. NO.:89), (SEQ. ID. NO.:90), [(SEQ. ID. NO.:91),] or (SEQ. ID. NO.:92).

91. (Twice Amended) An oligonucleotide primer for detecting a genetic predisposition for non-responsiveness to statin drug treatment in a human, said primer having a nucleotide sequence consisting [essentially of a nucleotide sequence] of (SEQ. ID. NO.:95), (SEQ. ID. NO.:96), (SEQ. ID. NO.:97), (SEQ. ID. NO.:98), (SEQ. ID. NO.:99), (SEQ. ID. NO.:100), (SEQ. ID. NO.:101), (SEQ. ID. NO.:102), (SEQ. ID. NO.:103), (SEQ. ID. NO.:104), (SEQ. ID. NO.:105), or (SEQ. ID. NO.:106).

92. (Twice Amended) An oligonucleotide primer set for detecting a genetic predisposition for non-responsiveness to statin drug treatment in a human, said primer set having a reverse primer having a nucleotide sequence consisting [essentially] of [the nucleotide sequence] 5'-GCA TCT GCC TTC AGC TAG ACA TTG-3' (SEQ. ID. NO.:1); and a forward primer having a nucleotide sequence consisting [essentially] of [the nucleotide sequence] 5'-TCT TCC AGA AGG GTG AGA TTC CAA-3' (SEQ. ID. NO.:2).

93. (Twice Amended) An oligonucleotide primer set for detecting a genetic predisposition for non-responsiveness to statin drug treatment in a human, having a forward primer having a nucleotide sequence consisting [essentially] of [a nucleotide sequence of] (SEQ. ID. NO.:2), (SEQ. ID. NO.:3), (SEQ. ID. NO.:4), (SEQ. ID. NO.:5), (SEQ. ID. NO.:6), (SEQ. ID. NO.:7), (SEQ. ID. NO.:8), (SEQ. ID. NO.:9), (SEQ. ID. NO.:11), (SEQ. ID. NO.:12), (SEQ. ID. NO.:13), (SEQ. ID. NO.:14), (SEQ. ID. NO.:15), (SEQ. ID. NO.:16), (SEQ. ID. NO.:17), (SEQ. ID. NO.:18), (SEQ. ID. NO.:19), (SEQ. ID. NO.:20), (SEQ. ID. NO.:21), (SEQ. ID. NO.:22), (SEQ. ID. NO.:23), (SEQ. ID. NO.:36), (SEQ. ID. NO.:37), (SEQ. ID. NO.:38), (SEQ. ID. NO.:39), (SEQ. ID. NO.:43), (SEQ. ID. NO.:45), (SEQ. ID. NO.:47), (SEQ. ID. NO.:48), (SEQ. ID. NO.:49), (SEQ. ID. NO.:50), (SEQ. ID. NO.:53), (SEQ. ID. NO.:54), (SEQ. ID. NO.:58), (SEQ. ID. NO.:59), (SEQ. ID. NO.:60), (SEQ. ID. NO.:61), (SEQ. ID. NO.:65)(SEQ. ID. NO.:66), (SEQ. ID. NO.:67), (SEQ. ID. NO.:68), (SEQ. ID. NO.:69).

ID. NO.:69), (SEQ. ID. NO.:70), (SEQ. ID. NO.:71), (SEQ. ID. NO.:72), (SEQ. ID. NO.:75), (SEQ. ID. NO.:76), (SEQ. ID. NO.:77), or (SEQ. ID. NO.:79);

and having a reverse primer having a nucleotide sequence consisting [essentially] of [a nucleotide sequence of] (SEQ. ID. NO.:1), (SEQ. ID. NO.:10), (SEQ. ID. NO.:24), (SEQ. ID. NO.:25), (SEQ. ID. NO.:26), (SEQ. ID. NO.:27), (SEQ. ID. NO.:28), (SEQ. ID. NO.:29), (SEQ. ID. NO.:30), (SEQ. ID. NO.:31), (SEQ. ID. NO.:32), (SEQ. ID. NO.:35), (SEQ. ID. NO.:40), (SEQ. ID. NO.:41), (SEQ. ID. NO.:42), (SEQ. ID. NO.:44), (SEQ. ID. NO.:46), (SEQ. ID. NO.:51), (SEQ. ID. NO.:52), (SEQ. ID. NO.:55), (SEQ. ID. NO.:56), (SEQ. ID. NO.:57), (SEQ. ID. NO.:62), (SEQ. ID. NO.:63), (SEQ. ID. NO.:64), (SEQ. ID. NO.:73), (SEQ. ID. NO.:74), or (SEQ. ID. NO.:78).

95. (Twice Amended) An oligonucleotide primer set for detecting a genetic predisposition for non-responsiveness to statin drug treatment in a human, having a forward primer having a nucleotide sequence consisting [essentially] of [a nucleotide sequence of] (SEQ. ID. NO.:82), (SEQ. ID. NO.:86), (SEQ. ID. NO.:88), (SEQ. ID. NO.:90), or (SEQ. ID. NO.:92);

and having a reverse primer having a nucleotide sequence consisting [essentially] of [a nucleotide sequence of] (SEQ. ID. NO.:83), (SEQ. ID. NO.:84), (SEQ. ID. NO.:85), [(SEQ. ID. NO.:87),] or (SEQ. ID. NO.:89)[, or (SEQ. ID. NO.:91)].

96. (Twice Amended) An oligonucleotide primer set for detecting a genetic predisposition for non-responsiveness to statin drug treatment in a human, having a forward primer having a nucleotide sequence consisting [essentially] of [a nucleotide sequence of] (SEQ. ID. NO.:95), (SEQ. ID. NO.:98), (SEQ. ID. NO.:99), (SEQ. ID. NO.:101), (SEQ. ID. NO.:102), (SEQ. ID. NO.:104), or (SEQ. ID. NO.:106);

and having a reverse primer having a nucleotide sequence consisting [essentially] of [a nucleotide sequence of] (SEQ. ID. NO.:96), (SEQ. ID. NO.:97), (SEQ. ID. NO.:100), (SEQ. ID. NO.:103), or (SEQ. ID. NO.:105).

97. (Twice Amended) A genetic testing kit comprising a primer having a nucleotide sequence consisting of [comprising a nucleotide sequence of] (SEQ. ID. NO.:1), (SEQ. ID. NO.:2), (SEQ. ID. NO.:3), (SEQ. ID. NO.:4), (SEQ. ID. NO.:5), (SEQ. ID. NO.:6), (SEQ. ID. NO.:7), (SEQ. ID. NO.:8), (SEQ. ID. NO.:9), (SEQ. ID. NO.:10), (SEQ. ID. NO.:11), (SEQ. ID. NO.:12), (SEQ. ID. NO.:13), (SEQ. ID. NO.:14), (SEQ. ID. NO.:15), (SEQ. ID. NO.:16), (SEQ. ID. NO.:17), (SEQ. ID. NO.:18), (SEQ. ID. NO.:19), (SEQ. ID. NO.:20), (SEQ. ID. NO.:21), (SEQ. ID. NO.:22), (SEQ. ID. NO.:23), (SEQ. ID. NO.:24), (SEQ. ID. NO.:25), (SEQ. ID. NO.:26), (SEQ. ID. NO.:27), (SEQ. ID. NO.:28), (SEQ. ID. NO.:29), (SEQ. ID. NO.:30), (SEQ. ID. NO.:31), (SEQ. ID. NO.:32), [(SEQ. ID. NO.:33), (SEQ. ID. NO.:34),] (SEQ. ID. NO.:35), (SEQ. ID. NO.:36), (SEQ. ID. NO.:37), (SEQ. ID. NO.:38), (SEQ. ID. NO.:39), (SEQ. ID. NO.:40), (SEQ. ID. NO.:41), (SEQ. ID. NO.:42), (SEQ. ID. NO.:43), (SEQ. ID. NO.:44), (SEQ. ID. NO.:45), (SEQ. ID. NO.:46), (SEQ. ID. NO.:47), (SEQ. ID. NO.:48), (SEQ. ID. NO.:49), (SEQ. ID. NO.:50), (SEQ. ID. NO.:51), (SEQ. ID. NO.:52), (SEQ. ID. NO.:53), (SEQ. ID. NO.:54), (SEQ. ID. NO.:55), (SEQ. ID. NO.:56), (SEQ. ID. NO.:57), (SEQ. ID. NO.:58), (SEQ. ID. NO.:59), (SEQ. ID. NO.:60), (SEQ. ID. NO.:61), (SEQ. ID. NO.:62), (SEQ. ID. NO.:63), (SEQ. ID. NO.:64), (SEQ. ID. NO.:65), (SEQ. ID. NO.:66), (SEQ. ID. NO.:67), (SEQ. ID. NO.:68), (SEQ. ID. NO.:69), (SEQ. ID. NO.:70), (SEQ. ID. NO.:71), (SEQ. ID. NO.:72), (SEQ. ID. NO.:73), (SEQ. ID. NO.:74), (SEQ. ID. NO.:75), (SEQ. ID. NO.:76), (SEQ. ID. NO.:77), (SEQ. ID. NO.:78), or (SEQ. ID. NO.:79)[, or comprising a sequence overlapping the sequence of any of these with respect to its position on the Nickerson reference sequence]; and

instructions for using the primer to detect a genetic predisposition in a human subject for non-responsiveness to treatment with a statin drug selected from the group consisting of lovastatin, pravastatin, and simvastatin.

98. (Twice Amended) A genetic testing kit comprising:

a primer having a nucleotide sequence consisting of [comprising a nucleotide sequence of] (SEQ. ID. NO.:82), (SEQ. ID. NO.:83), (SEQ. ID. NO.:84), (SEQ. ID. NO.:85), (SEQ. ID. NO.:86), [(SEQ. ID. NO.:87),] (SEQ. ID. NO.:88), (SEQ. ID. NO.:89), (SEQ. ID. NO.:90), [(SEQ. ID. NO.:91),] or (SEQ. ID. NO.:92)[, or comprising a sequence overlapping the sequence of any of these with respect to its position on the Nickerson reference sequence]; and

instructions for using the primer to detect a genetic predisposition in a human subject for non-responsiveness to treatment with a statin drug selected from the group consisting of lovastatin, pravastatin, and simvastatin.

99. (Twice Amended) A genetic testing kit comprising:

a primer having a nucleotide sequence consisting of [comprising a nucleotide sequence of] (SEQ. ID. NO.:95), (SEQ. ID. NO.:96), (SEQ. ID. NO.:97), (SEQ. ID. NO.:98), (SEQ. ID. NO.:99), (SEQ. ID. NO.:100), (SEQ. ID. NO.:101), (SEQ. ID. NO.:102), (SEQ. ID. NO.:103), (SEQ. ID. NO.:104), (SEQ. ID. NO.:105), or (SEQ. ID. NO.:106)[, or comprising a sequence overlapping the sequence of any of these with respect to its position on the Oka reference sequence]; and

instructions for using the primer to detect a genetic predisposition in a human subject for non-responsiveness to treatment with a statin drug selected from the group consisting of lovastatin, pravastatin, and simvastatin.

100. (Twice Amended) A genetic testing kit comprising:

a forward primer having a nucleotide sequence consisting of [comprising a nucleotide sequence of] (SEQ. ID. NO.:2), (SEQ. ID. NO.:3), (SEQ. ID. NO.:4), (SEQ. ID.

NO.:5), (SEQ. ID. NO.:6), (SEQ. ID. NO.:7), (SEQ. ID. NO.:8), (SEQ. ID. NO.:9), (SEQ. ID. NO.:11), (SEQ. ID. NO.:12), (SEQ. ID. NO.:13), (SEQ. ID. NO.:14), (SEQ. ID. NO.:15), (SEQ. ID. NO.:16), (SEQ. ID. NO.:17), (SEQ. ID. NO.:18), (SEQ. ID. NO.:19), (SEQ. ID. NO.:20), (SEQ. ID. NO.:21), (SEQ. ID. NO.:22), (SEQ. ID. NO.:23), (SEQ. ID. NO.:36), (SEQ. ID. NO.:37), (SEQ. ID. NO.:38), (SEQ. ID. NO.:39), (SEQ. ID. NO.:43), (SEQ. ID. NO.:45), (SEQ. ID. NO.:47), (SEQ. ID. NO.:48), (SEQ. ID. NO.:49), (SEQ. ID. NO.:50), (SEQ. ID. NO.:53), (SEQ. ID. NO.:54), (SEQ. ID. NO.:58), (SEQ. ID. NO.:59), (SEQ. ID. NO.:60), (SEQ. ID. NO.:61), (SEQ. ID. NO.:65), (SEQ. ID. NO.:66), (SEQ. ID. NO.:67), (SEQ. ID. NO.:68), (SEQ. ID. NO.:69), (SEQ. ID. NO.:70), (SEQ. ID. NO.:71), (SEQ. ID. NO.:72), (SEQ. ID. NO.:75), (SEQ. ID. NO.:76), (SEQ. ID. NO.:77), or (SEQ. ID. NO.:79)[, or comprising a sequence overlapping the sequence of any one of these with respect to its position on the Nickerson reference sequence];

a reverse primer having a nucleotide sequence consisting of [comprising a nucleotide sequence of] (SEQ. ID. NO.:1), (SEQ. ID. NO.:10), (SEQ. ID. NO.:24), (SEQ. ID. NO.:25), (SEQ. ID. NO.:26), (SEQ. ID. NO.:27), (SEQ. ID. NO.:28), (SEQ. ID. NO.:29), (SEQ. ID. NO.:30), (SEQ. ID. NO.:31), (SEQ. ID. NO.:32), (SEQ. ID. NO.:35), (SEQ. ID. NO.:40), (SEQ. ID. NO.:41), (SEQ. ID. NO.:42), (SEQ. ID. NO.:44), (SEQ. ID. NO.:46), (SEQ. ID. NO.:51), (SEQ. ID. NO.:52), (SEQ. ID. NO.:55), (SEQ. ID. NO.:56), (SEQ. ID. NO.:57), (SEQ. ID. NO.:62), (SEQ. ID. NO.:63), (SEQ. ID. NO.:64), (SEQ. ID. NO.:73), (SEQ. ID. NO.:74), or (SEQ. ID. NO.:78)[, or comprising a sequence overlapping the sequence of any of these with respect to its position on the Nickerson reference sequence]; and

instructions for using the forward and reverse primers to detect a genetic predisposition in a human subject for non-responsiveness to treatment with a statin drug selected from the group consisting of lovastatin, pravastatin, and simvastatin.

101. (Twice Amended) A genetic testing kit comprising:

a forward primer having a nucleotide sequence consisting of [comprising a nucleotide sequence of] (SEQ. ID. NO.:82), (SEQ. ID. NO.:86), (SEQ. ID. NO.:88), (SEQ.

ID. NO.:90), or (SEQ. ID. NO.:92)[, or comprising a sequence overlapping the sequence of any of these with respect to its position on the Nickerson reference sequence];

a reverse primer having a nucleotide sequence consisting of [comprising a nucleotide sequence of] (SEQ. ID. NO.:83), (SEQ. ID. NO.:84), (SEQ. ID. NO.:85), [(SEQ. ID. NO.:87),] or (SEQ. ID. NO.:89)[, or (SEQ. ID. NO.:91), or comprising a sequence overlapping the sequence of any of these with respect to its position on the Nickerson reference sequence]; and

instructions for using the forward and reverse primers to detect a genetic predisposition in a human subject for non-responsiveness to treatment with a statin drug selected from the group consisting of lovastatin, pravastatin, and simvastatin.

102. (Twice Amended) A genetic testing kit comprising:

a forward primer having a nucleotide sequence consisting of [comprising a nucleotide sequence of] (SEQ. ID. NO.:95), (SEQ. ID. NO.:98), (SEQ. ID. NO.:99), (SEQ. ID. NO.:101), (SEQ. ID. NO.:102), (SEQ. ID. NO.:104), or (SEQ. ID. NO.:106)[, or comprising a sequence overlapping the sequence of any of these with respect to its position on the Oka reference sequence];

a reverse primer having a nucleotide sequence consisting of [comprising a nucleotide sequence of] (SEQ. ID. NO.:96), (SEQ. ID. NO.:97), (SEQ. ID. NO.:100), (SEQ. ID. NO.:103), or (SEQ. ID. NO.:105)[, or comprising a sequence overlapping the sequence of any of these with respect to its position on the Oka reference sequence]; and

instructions for using the forward and reverse primers to detect a genetic predisposition in a human subject for non-responsiveness to treatment with a statin drug selected from the group consisting of lovastatin, pravastatin, and simvastatin.

New Claims 103-117 are added as follows.

--103.(New) The oligonucleotide primer of Claim 84, wherein the primer is labeled with a fluorescent dye.

104.(New) The oligonucleotide primer of Claim 85, wherein the primer is labeled with a fluorescent dye.

105.(New) The oligonucleotide primer of Claim 86, wherein the primer is labeled with a fluorescent dye.

106.(New) The oligonucleotide primer of Claim 89, wherein the primer is labeled with a fluorescent dye.

107.(New) The oligonucleotide primer of Claim 91, wherein the primer is labeled with a fluorescent dye.

108.(New) The oligonucleotide primer set of Claim 92, wherein the forward primer or the reverse primer, or both, is labeled with a fluorescent dye.

109.(New) The oligonucleotide primer set of Claim 93, wherein the forward primer or the reverse primer, or both, is labeled with a fluorescent dye.

110.(New) The oligonucleotide primer set of Claim 95, wherein the forward primer or the reverse primer, or both, is labeled with a fluorescent dye.

111.(New) The oligonucleotide primer set of Claim 96, wherein the forward primer or the reverse primer, or both, is labeled with a fluorescent dye.

112.(New) The genetic testing kit of Claim 97, wherein the primer is labeled with a fluorescent dye.

113.(New) The genetic testing kit of Claim 98, wherein the primer is labeled with a fluorescent dye.

114.(New) The genetic testing kit of Claim 99, wherein the primer is labeled with a fluorescent dye.

115.(New) The genetic testing kit of Claim 100, wherein the forward primer or the reverse primer, or both, is labeled with a fluorescent dye.

116.(New) The genetic testing kit of Claim 101, wherein the forward primer or the reverse primer, or both, is labeled with a fluorescent dye.

117.(New) The genetic testing kit of Claim 102, wherein the forward primer or the reverse primer, or both, is labeled with a fluorescent dye.--.